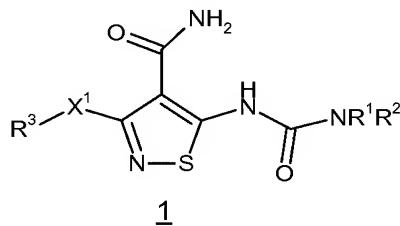


Listing of Claims

1. (Original) A method of treating a hyperproliferative disorder in a mammal which comprises administering to said mammal in need of such treatment, either simultaneously or sequentially, (i) a therapeutically effective amount of a taxane derivative, a platinum coordination complex selected from the group consisting of carboplatin, tetraplatin, and topotecan, a nucleoside analog selected from the group consisting of gemcitabine hydrochloride and 5_FU, an anthracycline, a topoisomerase selected from the group consisting of etoposide, teniposide, amsacrine, topotecan, and Camptosar®, an aromatase inhibitor; and (ii) a therapeutically effective amount of a compound of the formula 1



or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein:

wherein X¹ is O or S;

R¹ is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, -C(O)(C₁-C₁₀ alkyl), -(CH₂)_t(C₆-C₁₀ aryl), -(CH₂)_t(4-10 membered heterocyclic), -C(O)(CH₂)_t(C₆-C₁₀ aryl), or -C(O)(CH₂)_t(5-10 membered heterocyclic), wherein t is an integer from 0 to 5; said alkyl group optionally includes 1 or 2 hetero moieties selected from O, S and -N(R⁶)- with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said aryl and heterocyclic R¹ groups are optionally fused to a C₆-C₁₀ aryl group, a C₅-C₈ saturated cyclic group, or a 5-10 membered heterocyclic group; 1 or 2 carbon atoms in the foregoing heterocyclic moieties are optionally substituted by an oxo (=O) moiety; the -(CH₂)_t moieties of the foregoing R¹ groups optionally include a carbon-carbon double or triple bond where t is an integer from 2 to 5; and the foregoing R¹ groups, except H, are optionally substituted by 1 to 3 R⁴ groups;

R² is selected from the list of substituents provided in the definition of R¹, -SO₂(CH₂)_t(C₆-C₁₀ aryl), -SO₂(CH₂)_t(5-10 membered heterocyclic), and -OR⁵, t is an integer ranging from 0 to 5, the -(CH₂)_t moieties of the foregoing R² groups optionally include a carbon-carbon double or triple bond where t is an integer from 2 to 5, and the foregoing R² groups are optionally substituted by 1 to 3 R⁴ groups;

or R¹ and R² may be taken together with the nitrogen to which each is attached to form a 4-10 membered saturated monocyclic or polycyclic ring or a 5-10 membered heteroaryl ring, wherein said saturated and heteroaryl rings optionally include 1 or 2 heteroatoms selected from O, S and -N(R⁶)- in addition to the nitrogen to which R¹ and R² are attached, said -N(R⁶)- is optionally =N- or -N= where R¹ and R² are taken together as said heteroaryl group, said saturated ring optionally may be partially

unsaturated by including 1 or 2 carbon-carbon double bonds, and said saturated and heteroaryl rings, including the R⁶ group of said -N(R⁶)-, are optionally substituted by 1 to 3 R⁴ groups;

R³ is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, -(CH₂)_t(C₆-C₁₀ aryl), or -(CH₂)_t(5-10 membered heterocyclic), wherein t is an integer from 0 to 5; said alkyl group optionally includes 1 or 2 hetero moieties selected from O, S and -N(R⁶)- with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said aryl and heterocyclic R³ groups are optionally fused to a C₆-C₁₀ aryl group, a C₅-C₈ saturated cyclic group, or a 5-10 membered heterocyclic group; 1 or 2 carbon atoms in the foregoing heterocyclic moieties are optionally substituted by an oxo (=O) moiety; the -(CH₂)_t moieties of the foregoing R³ groups optionally include a carbon-carbon double or triple bond where t is an integer from 2 to 5, and the foregoing R³ groups are optionally substituted by 1 to 5 R⁴ groups;

each R⁴ is independently selected from C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, -OR⁵, -C(O)R⁵, -C(O)OR⁵, -NR⁸C(O)OR⁵, -OC(O)R⁵, -NR⁶SO₂R⁵, -SO₂NR⁵R⁶, -NR⁶C(O)R⁵, -C(O)NR⁵R⁶, -NR⁵R⁶, -S(O)_jR⁷ wherein j is an integer ranging from 0 to 2, -SO₃H, -NR⁵(CR⁶R⁷)_mOR⁶, -(CH₂)_t(C₆-C₁₀ aryl), -SO₂(CH₂)_t(C₆-C₁₀ aryl), -S(CH₂)_t(C₆-C₁₀ aryl), -O(CH₂)_t(C₆-C₁₀ aryl), -(CH₂)_t(5-10 membered heterocyclic), and -(CR⁶R⁷)_mOR⁶, wherein m is an integer from 1 to 5 and t is an integer from 0 to 5; said alkyl group optionally contains 1 or 2 hetero moieties selected from O, S and -N(R⁶)- with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said aryl and heterocyclic R⁴ groups are optionally fused to a C₆-C₁₀ aryl group, a C₅-C₈ saturated cyclic group, or a 5-10 membered heterocyclic group; 1 or 2 carbon atoms in the foregoing heterocyclic moieties are optionally substituted by an oxo (=O) moiety; and the alkyl, aryl and heterocyclic moieties of the foregoing R⁴ groups are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, -NR⁶SO₂R⁵, -SO₂NR⁵R⁶, -C(O)R⁵, -C(O)OR⁵, -OC(O)R⁵, -NR⁶C(O)R⁵, -C(O)NR⁵R⁶, -NR⁵R⁶, -(CR⁶R⁷)_mOR⁶ wherein m is an integer from 1 to 5, -OR⁵ and the substituents listed in the definition of R⁵;

each R⁵ is independently selected from H, C₁-C₁₀ alkyl, -(CH₂)_t(C₆-C₁₀ aryl), and -(CH₂)_t(5-10 membered heterocyclic), wherein t is an integer from 0 to 5; said alkyl group optionally includes 1 or 2 hetero moieties selected from O, S and -N(R⁶)- with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said aryl and heterocyclic R⁵ groups are optionally fused to a C₆-C₁₀ aryl group, a C₅-C₈ saturated cyclic group, or a 5-10 membered heterocyclic group; and the foregoing R⁵ substituents, except H, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, -C(O)R⁶, -C(O)OR⁶, -CO(O)R⁶, -NR⁶C(O)R⁷, -C(O)NR⁶R⁷, -NR⁶R⁷, hydroxy, C₁-C₆ alkyl, and C₁-C₆ alkoxy; and

each R⁶ and R⁷ is independently H or C₁-C₆ alkyl.

2. (Original) The method of claim 1, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel.
3. (Original) The method of claim 2, wherein the taxane is paclitaxel.
4. (Original) The method of claim 2, wherein the taxane is docetaxel.
5. (Original) The method according to claim 1, wherein the nucleoside analog is gemcitabine hydrochloride.
6. (Original) The method according to claim 1, wherein the platinum coordination complex is selected from the group consisting of carboplatin and tetraplatin.
7. (Original) The method according to claim 6, wherein the platinum coordination complex is carboplatin.
8. (Original) The method according to claim 7, wherein the platinum coordination complex is tetraplatin.
9. (Original) The method according to claim 1, wherein the nucleoside analog is gemcitabine hydrochloride.
10. (Original) The method according to claim 1, wherein the nucleoside analog is 5-FU.
11. (Original) The method according to claim 1, wherein the anthracycline is selected from the group consisting of doxorubicin, carminomycin and aclacinomycin.
12. (Original) The method according to claim 10, wherein the anthracycline is doxorubicin.
13. (Original) The method according to claim 1, wherein the topoisomerase is Camptosar®.
14. (Original) The method according to claim 1, wherein the aromatase inhibitor is selected from the group consisting of letrozole, vorazole, Aromasin® (exemestane), and anastrazole.
15. (Original) The method according to claim 14, wherein the aromatase inhibitor is selected from the group consisting of Aromasin® (exemestane), and anastrazole.

16. (Original) The method according to claim 15, wherein the aromatase inhibitor is Aromasin® (exemestane).
17. (Original) The method according to claim 15, wherein the aromatase inhibitor is anastrazole.
18. (Original) The method of claim 1, wherein the hyperproliferative disorder is cancer.
19. (Original) The method of claim 18, wherein said cancer is selected from the group consisting of brain, squamous cell, bladder, gastric, pancreatic, breast, head, neck, oesophageal, prostate, colorectal, lung, renal, kidney, ovarian, gynecological and thyroid cancer.
20. (Original) The method of claim 19, wherein said cancer is selected from the group consisting of prostate, breast, lung, colon and ovarian cancer.
21. (Original) The method of claim 20, wherein said cancer is selected from the group consisting of prostate, breast, and lung cancer.
22. (Original) The method of claim 21, wherein said breast cancer is metastatic breast cancer.
23. (Original) The method of claim 21, wherein said lung cancer is non-small cell lung cancer.
24. (Original) The method of claim 1, wherein said hyperproliferative disorder is non-cancerous.
25. (Original) The method of claim 24, wherein non-cancerous hyperproliferative disorder is benign hyperplasia of the skin or prostate.
26. (Original) The method of claim 1, wherein said compounds (i) and (ii) are administered simultaneously.
27. (Original) The method of claim 1, wherein said compounds (i) and (ii) are administered sequentially.

28. (Original) The method of claim 1, wherein R² of the compound of formula 1 is H and R¹ is C₁-C₁₀ alkyl optionally substituted by 1 or 2 substituents independently selected from -NR⁵R⁶, -NR⁵(CR⁶R⁷)OR⁶ and -(CH₂)_t(5-10 membered heterocyclic) wherein t is an integer from 0 to 5.

29. (Original) The method of claim 28, wherein R¹ of the compound of formula 1 is selected from propyl, butyl, pentyl and hexyl, and said R¹ groups are optionally substituted by dimethylamino, hydroxy, pyrrolidinyl, morpholino, and ethyl-(2-hydroxy-ethyl)-amino.

30. (Original) The method of claim 1, wherein R² of the compound of formula 1 is H and R¹ of the compound of formula 1 is -(CH₂)_t(5-10 membered heterocyclic), wherein t is an integer from 0 to 5; said heterocyclic group is optionally fused to a C₆-C₁₀ aryl group, a C₅-C₈ saturated cyclic group, or a 5-10 membered heterocyclic group; and said R¹ group, including the optionally fused portions of said R¹ group, is optionally substituted by 1 or 2 substituents independently selected from C₁-C₄ alkyl, hydroxy and hydroxymethyl.

31. (Original) The method of claim 30, wherein the heterocyclic moiety of said R¹ group is selected from morpholino, pyrrolidinyl, imidazolyl, piperazinyl, piperidinyl, and 2,5-diaza-bicyclo[2.2.1]hept-2-yl, the t variable of said R¹ group ranges from 2 to 5, and said R¹ group is optionally substituted by hydroxy, hydroxymethyl and methyl.

32. (Original) The method according to claim 1 wherein R³ of the compound of formula 1 is -(CH₂)_t(C₆-C₁₀ aryl) wherein t is an integer from 1 to 3 and said R³ group is optionally substituted by 1 to 4 R⁴ groups.

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33. (Original) The method according to claim 32 wherein R³ is benzyl optionally substituted by 1 to 4 substituents independently selected from halo and C₁-C₄ alkyl.

34. (Original) The method according to claim 33 wherein R³ is benzyl substituted by 1 to 4 substituents independently selected from methyl, fluoro, chloro and bromo.

35. (Original) The method according to claim 1, wherein the compound of formula 1 is selected from the group consisting of:

mesylate salt of 3-(4-Bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;
5-{3-[3-(4-Methyl-piperazin-1-yl)-propyl]-ureido}-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;
3-(4-Chloro-2,6-difluoro-benzyloxy)-5-(3-{4-[ethyl-(2-hydroxy-ethyl)-amino]-butyl}-ureido)-isothiazole-4-carboxylic acid amide;

3-(2-Fluoro-4-methyl-benzyl oxy)-5-[3-[3-(4-methyl-piperazin-1-yl)-propyl]-ureido]-isothiazole-4-carboxylic acid amide;

3-(2,5-Difluoro-4-methyl-benzyl oxy)-5-(3-4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-butyl)-ureido)-isothiazole-4-carboxylic acid amide;

3-(2,5-Difluoro-4-methyl-benzyl oxy)-5-[3-(6-dimethylamino-hexyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(2-Fluoro-4-methyl-benzyl oxy)-5-[3-(5-isopropylamino-pentyl)-ureido]-isothiazole-4-carboxylic acid amide;

hydrochloride salt of 3-(4-Bromo-2,6-difluoro-benzyl oxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzyl oxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzyl oxy)-5-{3-[3-(4-methyl-piperazin-1-yl)-propyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzyl oxy)-5-{3-[-(1-methyl-pyrrolidin-2-yl)-ethyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(2,6-Difluoro-4-methyl-benzyl oxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzyl oxy)-5-[3-(3-hydroxy-5-pyrrolidin-1-yl)-pentyl]-ureido)-isothiazole-4-carboxylic acid amide;

3-(2,5-Difluoro-4-methyl-benzyl oxy)-5-{3-[4-(3,4-dihydroxy-pyrrolidin-1-yl)-butyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzyl oxy)-5-{3-[4-(3,4-dihydroxy-pyrrolidin-1-yl)-butyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(2,5-Difluoro-4-methyl-benzyl oxy)-5-{3-[4-(2-hydroxymethyl-pyrrolidin-1-yl)-butyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzyl oxy)-5-{3-[4-(2-hydroxymethyl-pyrrolidin-1-yl)-butyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(2,5-Difluoro-4-methyl-benzyl oxy)-5-{3-[4-(3-hydroxy-pyrrolidin-1-yl)-butyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Bromo-2,6-difluoro-benzyl oxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(2,6-Difluoro-4-methyl-benzyl oxy)-5-[3-(4-hydroxy-5-piperidin-1-yl-pentyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(2,5-Difluoro-4-methyl-benzyl oxy)-5-{3-[4-(3-hydroxy-5-piperidin-1-yl-pentyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzylxy)-5-{3-[4-(2-hydroxymethyl-piperidin-1-yl)-butyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(2,5-Difluoro-4-methyl-benzylxy)-5-(3-{4-[ethyl-(2-hydroxy-ethyl)-amino]-butyl}-ureido)-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzylxy)-5-[3-(5-hydroxy-6-piperidin-1-yl)-hexyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Bromo-2,3,6-trifluoro-benzylxy)-5-{3-[3-(4-methyl-piperazin-1-yl)-propyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(2,6-Difluoro-4-methyl-benzylxy)-5-{3-[3-(4-methyl-piperazin-1-yl-propyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(2,6-Difluoro-4-methyl-benzylxy)-5-[3-(3-hydroxy-5-pyrrolidin-1-yl-pentyl)-ureido]-isothiazole-4-carboxylic acid amide;

5-[3-(4-Pyrrolidin-1-yl-butyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzylxy)-isothiazole-4-carboxylic acid amide;

5-[3-(3-Hydroxy-5-pyrrolidin-1-yl-pentyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzylxy)-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzylxy)-5-{3-[3-(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)-propyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,3,6-trifluoro-benzylxy)-5-{3-[3-(5-methyl-2,5-daza-bicyclo[2.2.1]hept-2-yl)-propyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,3,6-trifluoro-benzylxy)-5-{3-[2-(1-methyl-pyrrolidin-2-yl)-ethyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,3,6-trifluoro-benzylxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,3,6-trifluoro-benzylxy)-5-{3-[4-(2-hydroxymethyl-pyrrolidin-1-yl)-butyl]-ureido}-isothiazole-4-carboxylic acid amide;

5-{3-[2-(1-Methyl-pyrrolidin-2-yl)-ethyl]-ureido}-3-(2,3,6-trifluoro-4-methyl-benzylxy)-isothiazole-4-carboxylic acid amide;

5-[3-(4-Dimethylamino-butyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzylxy)-isothiazole-4-carboxylic acid amide;

5-[3-(3-Dimethylamino-propyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzylxy)-isothiazole-4-carboxylic acid amide;

5-[3-(3-Hydroxy-5-isopropylamino-pentyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzylxy)-isothiazole-4-carboxylic acid amide;

5-[3-(3-Isopropylamino-propyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzylxy)-isothiazole-4-carboxylic acid amide;

5-{3-[4-(4-Methyl-piperazin-1-yl)-butyl]-ureido}-3-(2,3,6-trifluoro-4-methyl-benzylxy)-isothiazole-4-carboxylic acid amide;

5-(3-{4-[4-(2-Hydroxy-ethyl)-piperazin-1-yl]-butyl}-ureido)-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;

5-[3-(3-Pyrrolidin-1-yl-propyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;

5-[3-(4-Hydroxy-5-piperidin-1-yl-pentyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,6-difluoro-benzyloxy)-5-[3-(4-imidazol-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

5-(3-{4-[Ethyl-(2-hydroxy-ethyl)-amino]-butyl}-ureido)-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-(2,3,6-trifluoro-benzyloxy)-5-{3-[4-(2-hydroxymethyl-piperidin-1-yl)-butyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,3,6-trifluoro-benzyloxy)-5-[3-(3-hydroxy-5-pyrrolidin-1-yl-pentyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Bromo-2,6-difluoro-benzyloxy)-5-{3-[3-(4-methyl-piperazin-1-yl)-propyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(2,6-Difluoro-4-methyl-benzyloxy)-5-{3-[2-(1-methyl-pyrrolidin-2-yl)-ethyl]-ureido}-isothiazole-4-carboxylic acid amide;

3-(2,6-Difluoro-4-methyl-benzyloxy)-5-[3-(4-dimethylamino-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Bromo-2,3,6-trifluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,3,6-trifluoro-benzyloxy)-5-[3-(4-imidazol-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,3,6-difluoro-benzyloxy)-5-(3-{3-[ethyl-(2-hydroxy-ethyl)-amino]-propyl}-ureido)-isothiazole-4-carboxylic acid amide;

3-(4-Chloro-2,3,6-trifluoro-benzyloxy)-5-(3-{3-[ethyl-(2-hydroxy-ethyl)-amino]-propyl}-ureido)-isothiazole-4-carboxylic acid amide;

5-[3-(3-Methylamino-propyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;

5-[3-(3-Amino-propyl)-3-methyl-ureido]-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;

5-[3-(4-Diethylamino-butyl)-ureido]-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;

3-(2,6-Difluoro-4-methyl-benzyloxy)-5-[3-(3-pyrrolidin-1-yl-propyl)-ureido]-isothiazole-4-carboxylic acid amide;

3-(3-Chloro-2,6-difluoro-4-methyl-benzyloxy)-5-[3-(4-dimethylamino-butyl)-ureido]-isothiazole-4-carboxylic acid amide;
5-(3-{4-[Bis-(2-hydroxy-ethyl)-amino]-butyl}-ureido)-3-(2,6-difluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;
and the pharmaceutically acceptable salts, prodrugs and solvates of said compounds.

36. (Original) The method according to claim 35, wherein the compound of formula 1 is selected from the group consisting of:
3-(4-Bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;
mesylate salt of 3-(4-Bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;
5-{3-[3-(4-Methyl-piperazin-1-yl)-propyl]-ureido}-3-(2,3,6-trifluoro-4-methyl-benzyloxy)-isothiazole-4-carboxylic acid amide;
3-(4-Chloro-2,6-difluoro-benzyloxy)-5-(3-{4-[ethyl-(2-hydroxy-ethyl)-amino]-butyl}-ureido)-isothiazole-4-carboxylic acid amide;
3-(2-Fluoro-4-methyl-benzyloxy)-5-{3-[3-(4-methyl-piperazin-1-yl)-propyl]-ureido}-isothiazole-4-carboxylic acid amide;
3-(2,5-Difluoro-4-methyl-benzyloxy)-5-(3-4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-butyl)-ureido)-isothiazole-4-carboxylic acid amide;
3-(2,5-Difluoro-4-methyl-benzyloxy)-5-[3-(6-dimethylamino-hexyl)-ureido]-isothiazole-4-carboxylic acid amide;
3-(2-Fluoro-4-methyl-benzyloxy)-5-[3-(5-isopropylamino-pentyl)-ureido]-isothiazole-4-carboxylic acid amide;
hydrochloride salt of 3-(4-Bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;
and the pharmaceutically acceptable salts, prodrugs and solvates of said compounds.

37. (Original) The method according to claim 36, wherein the compound of formula 1 is selected from the group consisting of:
3-(4-Bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;
mesylate salt of 3-(4-Bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;
hydrochloride salt of 3-(4-Bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide;
and the pharmaceutically acceptable salts, prodrugs and solvates of said compounds.

38. (Original) The method according to claim 37, wherein the compound of formula 1 is hydrochloride salt of 3-(4-Bromo-2,6-difluoro-benzylxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide; and the pharmaceutically acceptable salts, prodrugs and solvates of said compound.

39. (Original) The method of claim 38, comprising a therapeutically effective amount of paclitaxel.

40. (Original) The method of claim 38, comprising a therapeutically effective amount of gemcitabine hydrochloride.

41. (Original) The method of claim 38, comprising a therapeutically effective amount of carboplatin.

42. (Cancel).

43. (Original) The method of claim 38, comprising a therapeutically effective amount of doxorubicin.

44. (Original) The method according to claim 38, comprising a therapeutically effective amount of Camptosar®.

45. (Original) The method according to claim 38, comprising a therapeutically effective amount of Aromasin®.

46. (Original) The method according to claim 38, comprising a therapeutically effective amount of anastrazole.

47. (Original) A pharmaceutical composition for the treatment of a hyperproliferative disorder in a mammal which comprises (i) a therapeutically effective amount of a taxane derivative, a platinum coordination complex selected from the group consisting of carboplatin, tetraplatin, and topotecan, a nucleoside analog selected from the group consisting of gemcitabine hydrochloride and 5-FU, an anthracycline, a topoisomerase selected from the group consisting of etoposide, teniposide, amsacrine, topotecan, and Camptosar®, an aromatase inhibitor; and (ii) a therapeutically effective amount of a compound of the formula 1, in combination with one or more pharmaceutically acceptable carriers or vehicles.

48 to 66. (Cancel)

67. (Original) A method of treating a hyperproliferative disorder in a mammal which comprises administering to said mammal in need of such treatment, either simultaneously or sequentially, (i) a therapeutically effective amount of a taxane derivative, a platinum coordination complex selected from the group consisting of carboplatin, tetraplatin, and topotecan, a nucleoside analog selected from the group consisting of gemcitabine hydrochloride and 5-FU, an anthracycline, a topoisomerase selected from the group consisting of etoposide, teniposide, amsacrine, topotecan, and Camptosar[®], an aromatase inhibitor; and (ii) a therapeutically effective amount of the hydrochloride salt of 3-(4-Bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide.

68 to 92. (Cancel)